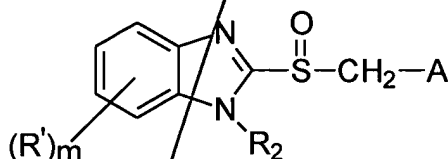


CLAIMS

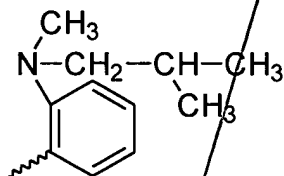
I claim:

1. An oral pharmaceutical preparation comprising:
- an inert nucleus;
 - a soluble active layer or layer which disintegrates rapidly in water, made from a single aqueous or hydroalcoholic solution-suspension which comprises:
 - an active ingredient of anti-ulcer activity of general formula I

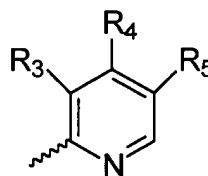


wherein:

A is:



or



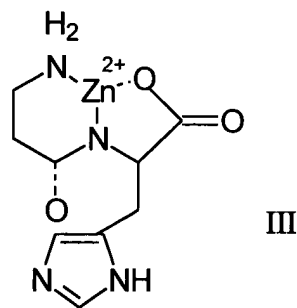
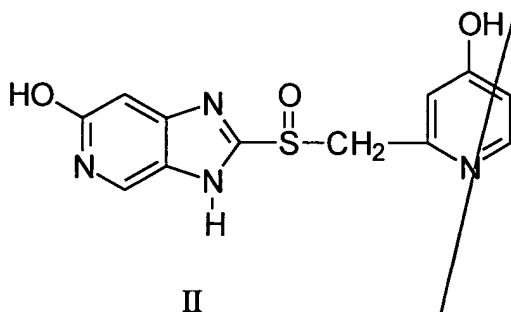
in which: R^3 and R^5 are the same or different, and may be hydrogen, alkyl, alkoxy, or alkoxyalkoxy;

R^4 is hydrogen, alkyl, alkoxy which can optionally be fluorated, alkoxyalkoxy, or alkoxycycloalkyl;

R¹ is hydrogen, alkyl, halogen, cyano, carboxy, carboalkoxy, carboalkoxyalkyl, carbamoyl, carbamoylalkyl, hydroxy, alkoxy, hydroxyalkyl, trifluoromethyl, acyl, carbamoyloxy, nitro, acyloxy, aryl, aryloxy, alkylthio or alkylsulphinyl;

R² is hydrogen, alkyl, acyl, carboalkoxy, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, alkylcarbonilmethyl, alkoxycarbonilmethyl or alkylsulfonil; and, m is a whole number from 0 to 4;

or of formula II or III,



and

- at least one pharmaceutically acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, a surface-active agent, a filling material and a disintegrating-swelling excipient; and

c) a gastro-resistant outer coating made from a solution which includes:

- an enteric coating polymer; and

- at least one excipient chosen from the group which includes: a plasticizer, a surface-active agent, a pigment and a lubricant.

2. The pharmaceutical preparation of claim 1, wherein the inert nucleus is a neutral spherical microgranule which includes in its composition at least two of: sorbitol, mannitol, saccharose, starch, microcrystalline cellulose, lactose, glucose, trehalose, maltitol or fructose.

3. The pharmaceutical preparation of claim 1, wherein the inert nucleus has an initial size between 200 and 1800 micrometers, preferably between 600-900 micrometers.

4. The pharmaceutical preparation of claim 1, wherein the binder in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of saccharose, starch, methyl cellulose, CMC, HPC, HPMC, polyvinyl pyrrolidone (PVP), dextrin or gum arabic, dissolved in water, ethanol, or a mixture of both at 50% (v/v).

5. The pharmaceutical preparation of claim 1, wherein the compound of alkaline reaction in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of trisodium phosphate, disodium phosphate, magnesium oxide, magnesium hydroxide, magnesium carbonate, aluminium hydroxide, carbonate, phosphate or citrate of aluminium, calcium, sodium or potassium, the mixed compounds of aluminium/magnesium $\text{Al}_2\text{O}_3 \cdot 6\text{MgO} \cdot \text{CO}_2 \cdot 12\text{H}_2\text{O}$ or $\text{MgO} \cdot \text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot n\text{H}_2\text{O}$ and amino acids with alkaline reaction.

6. The pharmaceutical preparation of claim 1, wherein the surface-active agent in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of sodium lauryl sulphate, polysorbate, poloxamer or other ionic and non-ionic surface-active agents.

5

7. The pharmaceutical preparation of claim 1, wherein said filling material in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of lactose, starch, saccharose and microcrystalline cellulose.

8. The pharmaceutical preparation of claim 1, wherein said disintegrating-swelling excipient in said aqueous or hydroalcoholic solution suspension is selected from the group consisting of starch, CMCCa, sodium glycolate starch and L-HPC.

9. The pharmaceutical preparation of claim 1, wherein said enteric coating polymer in said external gastro-resistant coating is selected from the group consisting of methyl cellulose, HEC, HBC, HPMC, ethyl cellulose, HMC, HPC, polyoxyethylene glycol, castor oil, cellulose phthalic acetate, phthalate of HPMC, succinate acetate of HMC, sodium carboxymethylamylopectin, chitosan, alginic acid, carrageenans, galactomannons, tragacanth, shellac, agar-agar, gum arabic, guar gum, xanthan gum, polyacrylic acids, methacrylics and their salts, PVA, polyethylene and polypropylene oxides and mixtures thereof.

10. The pharmaceutical preparation of claim 1, wherein said plasticizer in said external gastro-resistant coating is selected from the group consisting of TEC, PEG, cetyl alcohol and stearyl alcohol.

5 11. The pharmaceutical preparation of claim 1, wherein said surface-active agent present in said external gastro-resistant coating layer is selected from the group consisting of sodium lauryl sulphate, polysorbate and poloxamer.

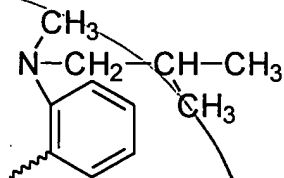
12. The pharmaceutical preparation of claim 1, wherein said pigment in said external gastro-resistant coating layer is selected from the group consisting of titanium dioxide and iron sesquioxide.

13. The pharmaceutical preparation of claim 1, wherein said lubricant in said external gastro-resistant coating layer is selected from the group consisting of talc, magnesium stearate and glyceryl monostearate.

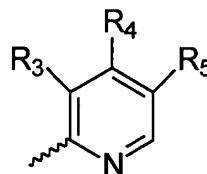
14. A process for making an oral pharmaceutical preparation comprising:
a) coating inert nuclei to form a layer thereon by spraying aqueous or hydroalcoholic suspension-solution, which comprises:

20 - an active ingredient of anti-ulcer activity of general formula I wherein:

A is:



or



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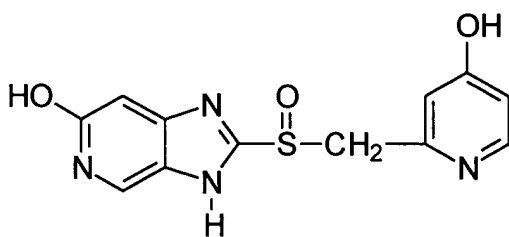
wherein R^3 and R^5 are the same or different, and may be hydrogen, alkyl, alkoxy, or alkoxyalkoxy;

R^4 is hydrogen, alkyl, alkoxy which can be fluorated, alkoxyalkoxy, or optionally alkoxyalkoxy;

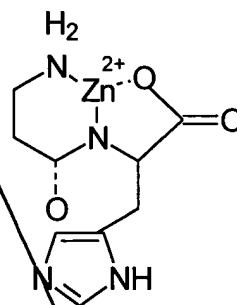
R^1 is hydrogen, alkyl, halogen, cyano, carboxy, carboalkoxy, carboalkoxyalkyl, carbamoyl, carbamoylalkyl, hydroxy, alkoxy, hydroxyalkyl, trifluoromethyl, acyl, carbamoyloxy, nitro, acyloxy, aryl, aryloxy, alkylthio or alkylsulphinyl;

R^2 is hydrogen, alkyl, acyl, carboalkoxy, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, alkylcarbonilmethyl, alkoxyalkylmethyl or alkylsulfonil; and, m is a whole number from 0 a 4;

or of general formula II or III,



II



III

20

and

- at least one pharmaceutically acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, surface-active agents, a filling material and disintegrating-swelling excipients;

5 b) drying the active layer formed during said spraying to form charged nuclei; and

 c) coating the charged nuclei by spraying a solution which contains an enteric coating polymer with at least one pharmaceutically acceptable excipient selected from the group comprising: a plasticizer, a surface-active agent, a pigment and a lubricant, to form an gastro-resistant external coating layer.

15 15. The process of claim 14 further comprising drying the coated charged nuclei.

15 16. The process of claim 14, wherein said binder in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of saccharose, starch, methylcellulose, CMC, HPC, HPMC, polyvinyl pyrrolidone (PVP), dextrin or gum arabic, either alone or mixed, dissolved in water, ethanol or a mixture of both at 50% (v/v).

20 17. The process of claim 14, wherein said compound of alkaline reaction in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of

trisodium phosphate, disodium phosphate, magnesium oxide, magnesium hydroxide, magnesium carbonate, aluminium hydroxide, carbonate, phosphate or citrate of aluminium, calcium, sodium or potassium, and the mixed compounds of aluminium/magnesium $\text{Al}_2\text{O}_3 \cdot 6\text{MgO} \cdot \text{CO}_2 \cdot 12\text{H}_2\text{O}$ or $\text{MgO} \cdot \text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot n\text{H}_2\text{O}$ and amino acids with alkaline reaction.

18. The process of claim 14, wherein said surface-active agent present in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of sodium lauryl sulphate, polysorbate, poloxamer or other ionic and non-ionic surface-active agents.

19. The process of claim 14, wherein said filling material in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of lactose, starch, saccharose and microcrystalline cellulose.

20. The process of claim 14, wherein said disintegrating-swelling excipient in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of starch, CMCCa, sodium glycolate starch and L-HPC.

21. The process of claim 14, wherein said enteric coating polymer in said external gastro-resistant coating is selected from the group consisting of methyl cellulose, HEC, HBC, HPMC, ethyl cellulose, HMC, HPC, polyoxyethylene glycol, castor oil, cellulose

phthalic acetate, phthalate of HPMC, succinate acetate of HMC, sodium carboxymethylamylopectin, chitosan, alginic acid, carrageenans, galactomannons, tragacanth, shellac, agar-agar, gum arabic, guar gum, xanthan gum, polyacrylic acids, methacrylics and their salts, PVA, polyethylene and polypropylene oxides and mixtures thereof.

22. The process of claim 14, wherein said plasticizer in said external gastro-resistant coating is selected from the group consisting of TEC, PEG, cetyl and stearyl alcohol.

23. The process of claim 14, wherein said surface-active agent in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of sodium lauryl sulphate, polysorbate and poloxamer.

24. The process of claim 14, wherein said pigment in said external gastro-resistant coating layer is selected from the group consisting of titanium dioxide and iron sesquioxide.

25. The process of claim 14, wherein said lubricant in said external gastro-resistant coating layer is selected from the group consisting of talc, magnesium stearate and glyceryl monostearate.

26. The pharmaceutical preparation of claim 1 wherein the filling material is

selected from the group consisting of mannitol, sorbitol or gelatin.

27. The pharmaceutical preparation of claim 1 wherein the alkaline reacting compound is selected from the group consisting of sodium, potassium, aluminum or calcium acetate; sodium, potassium, aluminum or calcium glycerophosphate; (tris)-hydroxymethylaminemethane (tromethamine), N-methylglucamine, 2-amine-2-methyl-1, 3-propanediol; 2-amine-2-methyl-1propanol; sodium, potassium, magnesium, calcium, aluminum or aluminum hydroxide salts of aminoacids like lysine, glutamic acid, glycine or pyrimidinecarboxylic acids, like nicotinic acid, salts derived from organic or weak inorganic acids and bases like guanidine and basic aminoacids like arginine, histidine, lysine and triptophane.

28. The pharmaceutical preparation of claim 1 wherein the enteric coating polymer is selected from the group consisting of HPMC acetate succinate, polyvinyl acetate phthalate, and cellulose acetate trimethylate.

29. The pharmaceutical preparation of claim 1 wherein the plasticizer is selected from the group consisting of diethyl phthalate, dibutyl phthalate, dimethyl phthalate, dioctyl adipate, dioctyl phthalate, dioctyl terephthalate, butyloctyl phthalate, triethylene glycol di-2-ethylhexanoate, trioctylmethyleate, glyceryl triacetate, glyceryl tripropionate, 2,2,4-trimethyl-1,3-pentanedioaldiisobutyrate.

30. The process of claim 14 wherein the filling material is selected from the group consisting of mannitol, sorbitol or gelatin.

31. The process of claim 14 wherein the alkaline reacting compound is selected from the group consisting of sodium, potassium, aluminum or calcium acetate; sodium, potassium, aluminum or calcium glycerophosphate; (tris)-hydroxymethylaminemethane (tromethamine); N-methylglucamine, 2-amine-2-methyl-1, 3-propanediol; 2-amine-2-methyl-1propanole; sodium, potassium, magnesium, calcium, aluminum or aluminum hydroxide salts of aminoacids like lysine, glutamic acid, glycine or pyrimidinecarboxylic acids, like nicotinic acid, salts derived from organic or weak inorganic acids and bases like guanidine and basic aminoacids like arginine, histidine, lysine and triptophane.

32. The process of claim 14 wherein the enteric coating polymer is selected from the group consisting of HPMC acetate succinate, polyvinyl acetate phthalate and, cellulose acetate trimethylate.

33. The process of claim 14 wherein the plasticizer is selected from the group consisting of diethyl phthalate, dibutyl phthalate, dimethyl phthalate, dioctyl adipate, dioctyl phthalate, dioctyl terephthalate, butyloctyl phthalate, triethylene glycol di-2-

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add a2
ethylhexanoate, trioctylmethyle, glyceryl triacetate, glyceryl tripropionate and, 2,2,4-trimethyl-1, 3-pentanediodiisobutyrate.

009270-42976460

add a3

add C1

add 37

add E1